Scientific Opinion on the annual post-market environmental monitoring (PMEM) report from Monsanto Europe S.A. on the cultivation of genetically modified maize MON 810 in 2012

EFSA Panel

Abstract: Following a request from the European Commission, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) assessed the post-market environmental monitoring (PMEM) report for the 2012 growing season of maize MON 810 provided by Monsanto Europe S.A. The EFSA GMO Panel noted that the applicant used a similar methodology as the one previously established for monitoring maize MON 810 in 2009, 2010 and 2011. The EFSA GMO Panel therefore focused its assessment on the novel datasets specific to the 2012 growing season of maize MON 810, and not on the methodology. The data submitted by the applicant in its 2012 PMEM report do not indicate any adverse effects on human and animal health or the environment arising from maize MON 810 cultivation in 2012. However, having already highlighted the poor sensitivity of the methodology followed by the applicant, the EFSA GMO Panel strongly reiterates its previous recommendations for the improvement of the methodology. In addition, the EFSA GMO Panel recommends that the applicant: (1) further investigates effects observed during the monitoring of baseline susceptibility of target pests in Spain; (2) follow-up possible adverse effects of maize MON 810 on rove beetles.

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SCIENTIFIC OPINION

Scientific Opinion on the annual post-market environmental monitoring (PMEM) report from Monsanto Europe S.A. on the cultivation of genetically modified maize MON 810 in 2012[1]

EFSA Panel on Genetically Modified Organisms (GMO)[2,3]

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ABSTRACT

Following a request from the European Commission, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) assessed the post-market environmental monitoring (PMEM) report for the 2012 growing season of maize MON 810 provided by Monsanto Europe S.A. The EFSA GMO Panel noted that the applicant used a similar methodology as the one previously established for monitoring maize MON 810 in 2009, 2010 and 2011. The EFSA GMO Panel therefore focused its assessment on the novel datasets specific to the 2012 growing season of maize MON 810, and not on the methodology. The data submitted by the applicant in its 2012 PMEM report do not indicate any adverse effects on human and animal health or the environment arising from maize MON 810 cultivation in 2012. However, having already highlighted the poor sensitivity of the methodology followed by the applicant, the EFSA GMO Panel strongly reiterates its previous recommendations for the improvement of the methodology. In addition, the EFSA GMO Panel recommends that the applicant: (1) further investigates effects observed during the monitoring of baseline susceptibility of target pests in Spain; (2) follow-up possible adverse effects of maize MON 810 on rove beetles.

KEY WORDS

annual PMEM report, cultivation, case-specific monitoring, general surveillance, insect-resistance management, maize, MON 810

[1] On request from European Commission, Question No EFSA-Q-2014-00179, adopted on 22 May 2014.

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SUMMARY

Following a request from the European Commission, the Panel on Genetically Modified Organisms of the European Food Safety Authority (EFSA GMO Panel) assessed the post-market environmental monitoring (PMEM) report for the 2012 growing season of maize MON 810 provided by Monsanto Europe S.A.

The EFSA GMO Panel firstly noted that the applicant followed a similar methodological approach for both Case-Specific Monitoring (CSM) and General Surveillance (GS) of maize MON 810 as in its previous PMEM reports. Subsequently, considering the unchanged methodology for PMEM of maize MON 810 in 2012, the EFSA GMO Panel focused its assessment on the novel datasets specific to the 2012 growing season of maize MON 810 (i.e. data from monitoring changes in baseline susceptibility of target pests, farmer questionnaires, information on refugia compliance in Spain and Portugal, and outcomes of the literature review). These data, submitted by the applicant in its 2012 PMEM report, do not indicate any adverse effects on human and animal health or the environment arising from maize MON 810 cultivation in 2012.

However, the sensitivity of the methodology is still considered too low for an early detection of possible adverse effects. Hence, the Panel's previous recommendations for improvement of the PMEM of maize MON 810 are repeated, in particular the recommendation for annual sampling of both target pests in areas of high maize MON 810 adoption rate.

In addition, the EFSA GMO Panel recommends that the applicant: (1) further investigates effects observed during the monitoring of baseline susceptibility of target pests in Spain; (2) follow-up possible adverse effects of maize MON 810 on rove beetles.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION AND EFSA

The placing on the market for cultivation of maize MON 810 in the EU is authorised since 1998 through Commission Decision 98/294/EC of 22 April 1998 (EC, 1998) and the consent granted on 3 August 1998 by the Competent Authority of France.

Following the request by the applicant for the renewal of the authorisation for placing maize MON 810 on the market, the EFSA GMO Panel adopted a scientific opinion on the renewal under Regulation (EC) No 1829/2003 of maize MON 810 for import, processing for food & feed uses and cultivation in June 2009 (EFSA, 2009). The EFSA GMO Panel concluded that "*maize MON 810 is unlikely to have any adverse effect on the environment in the context of its intended uses, especially if appropriate management measures are put in place in order to mitigate possible exposure of non-target (NT) Lepidoptera*". The EFSA GMO Panel recommended that, especially in areas of abundance of non-target Lepidoptera populations, the adoption of the cultivation of maize MON 810 be accompanied by management measures in order to mitigate the possible exposure of these species to maize MON 810 pollen. In addition, the EFSA GMO Panel advised that resistance management strategies continue to be employed and that the evolution of resistance in lepidopteran target pests continue to be monitored in order to detect potential changes in resistance levels in pest populations. The EFSA GMO Panel agreed with the overall approach and methodology proposed by the applicant for general surveillance, but advised the applicant to describe in more detail how information will be collected that could be used to assess if the intended uses of maize MON 810 are having unanticipated adverse environmental effects.

From 2005 onwards, the applicant submitted to the European Commission PMEM reports on the cultivation of maize MON 810 according to the provisions of Directive 2001/18/EC (EC, 2001).

From 2010 onwards, the EFSA GMO Panel received the requests from the European Commission to assess the annual PMEM reports submitted by Monsanto on the cultivation of maize MON 810. The EFSA GMO Panel therefore adopted a scientific opinion on the 2009, 2010 and 2011 PMEM reports (EFSA GMO Panel, 2011b, 2012a, 2013a). From the data submitted by the applicant in its previous reports, the EFSA GMO Panel did not identify adverse effects on the environment, human and animal health due to maize MON 810 cultivation. However, the EFSA GMO Panel noted shortcomings in the methodology and hence made recommendations for improvement of the PMEM of maize MON 810.

On 4 March 2014, the EFSA GMO Panel received from the European Commission a request to assess the PMEM report submitted by Monsanto on the cultivation of maize MON 810 in 2012 taking into consideration comments from Member States on the report.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION AND EFSA

On 4 March 2014, the EFSA GMO Panel was asked by the European Commission "*to evaluate the findings of the monitoring activities, taking into consideration the comments received from Member States and to assess the appropriateness of the methodology if this is found to differ compared to the previous season*."

ASSESSMENT

1. Introduction

Following the terms of reference of the mandate from the European Commission, the EFSA GMO Panel considered whether the methodology used by the applicant to monitor maize MON 810 over the 2012 growing season differs from the methodology applied by the applicant in its PMEM reports for the 2009, 2010 and 2011 growing seasons of maize MON 810 (EFSA GMO Panel, 2011b, 2012a, 2013a).

In addition, the EFSA GMO Panel assessed the novel datasets specific to the 2012 growing season (e.g. Spanish datasets from monitoring the baseline susceptibility of target pests, questionnaires answered by selected farmers in the European Union countries where maize MON 810 was cultivated in 2012, outcomes of the search for peer-reviewed publications on the safety of maize MON 810 and the Cry1Ab protein).

The EFSA GMO Panel also considered the comments from Member States on the PMEM report on the 2012 growing season of maize MON 810 (hereafter referred to as '2012 PMEM report').

2. Overview of information provided by the applicant

The 2012 PMEM report shows the same structure as the previous reports and contains the following information:

- an insect resistance management (IRM) plan[4] consisting of (1) the 'high dose-refuge' strategy, including studies on farmers' compliance with non-Bt refugia; (2) the monitoring for changes in baseline susceptibility of target pests; (3) a communication plan with farmers; (4) a remedial action plan in the event of any confirmed evolution of pest resistance;
- the survey[5] based on 249 questionnaires received from farmers in five European countries (i.e. 22 in the Czech Republic, 175 in Spain, 41 in Portugal, 10 in Romania and 1 in Slovakia);
- a list[6] of peer-reviewed publications pertaining to the safety of maize MON 810 and/or the Cry1Ab protein published between June 2012 and beginning of June 2013;
- company stewardship activities; and
- alerts on environmental issues by the authorities and existing networks.

The 2012 PMEM report is published online:
http://ec.europa.eu/food/plant/gmo/reports_studies/report_2012_mon_810_en.htm

3. Assessment

In its 2012 PMEM report, the applicant clearly states that the previously established methodologies were followed notwithstanding the EFSA GMO Panel recommendations to improve the methodology for PMEM of maize MON 810.

The EFSA GMO Panel acknowledges that there was not enough time for the applicant to implement the latest EFSA recommendations (EFSA GMO Panel, 2013a). However, the EFSA GMO Panel also points out that its previous recommendations for improvement of the PMEM methodology of maize MON 810, as in its opinions on 2009 and 2010 PMEM reports, have yet to be implemented (EFSA GMO Panel, 2011b, 2012a). Therefore, having already highlighted the poor sensitivity of the methodology followed by the applicant, the EFSA GMO Panel reiterates all its recommendations

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[4] MON 810 2012 PMEM report, Appendix 6.
[5] MON 810 2012 PMEM report, Appendix 1.
[6] MON 810 2012 PMEM report, Appendices 5.1 and 5.2.

(EFSA GMO Panel, 2011b, 2012a, 2013a) for consideration by the applicant in the PMEM plan and forthcoming PMEM reports.

Consequently, considering the unchanged methodology for PMEM of maize MON 810 in 2012, the EFSA GMO Panel focused its assessment on the novel datasets specific to the 2012 growing season of maize MON 810, i.e.

(1) data from the specific survey by Antama (the Spanish Foundation supporting the use of new technologies in agriculture) and the inspection campaign on non-Bt refugia compliance by Spanish and Portuguese farmers, respectively;

(2) Spanish data[7] from monitoring changes in baseline susceptibility of target pests (i.e. European Corn Borer (ECB; *Ostrinia nubilalis* Hübner) and Mediterranean Corn Borer (MCB; *Sesamia nonagrioides* Lefebvre)) in 2012;

(3) farmer responses to questionnaires in the five EU countries where maize MON 810 was cultivated in 2012;

(4) the list of peer-reviewed publications pertaining to the safety of maize MON 810 and the Cry1Ab protein for human and animal health and the environment.

3.1. Implementation of non-Bt refugia

The EFSA GMO Panel analysed the results of the survey by Antama addressing the implementation of non-Bt refugia by 110 Spanish farmers (i.e. in the Ebro Valley) who cultivated maize MON 810 in 2012. It concluded that 7 % of the farmers growing maize MON 810 in 2012 did not plant a refuge area. The reasons given by the farmers for not planting a refuge area were: "*(1) they considered their farms to be small farms; (2) sowing is easier (with Bt-maize); (3) corn borers cause significant losses*."

In 2012, the Portuguese inspection services visited the farmers cultivating maize MON 810 for control of good implementation of Portuguese law pertaining to cultivation of GM varieties. They concluded that there was full compliance with refuge implementation.

As in 2011, the 2012 PMEM report still shows partial non-compliance with the implementation of non-Bt refugia in Spain, which was confirmed by the farmer questionnaires.[8] The EFSA GMO Panel therefore recommends that the applicant should maintain its efforts to increase the level of compliance, especially in regions of high maize MON 810 uptake.

3.2. Monitoring for changes in baseline susceptibility of target pests

In line with its previous recommendation to focus the sampling of target pests in areas of high maize MON 810 uptake (EFSA GMO Panel, 2013a), the EFSA GMO Panel assessed the datasets[9] for the monitoring of changes in baseline susceptibility of the target pests in Spain. In addition to the aforementioned comments from Member States, a report[10] of the French Haut Conseil des Biotechnologies (HCB) was considered which carried out a specific analysis on the susceptibility of target pests over time.

In its 2012 PMEM report, the applicant acknowledged that "*the variation in Cry1Ab susceptibility (MIC50 and MIC90) of ECB collected in the field during the campaign 2012-2013 (…) reflected natural variation in Bt susceptibility among ECB origins.*" Overall, Monsanto concluded that the 2012 data analysis did not indicate a decrease of the target pest susceptibility to Cry1Ab protein.

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[7] MON 810 2012 PMEM report, Appendices 7 and 8.
[8] MON 810 2012 PMEM report, Appendix 1.
[9] MON 810 2012 PMEM report, Appendices 7 and 8.
[10] Available online: http://www.hautconseildesbiotechnologies.fr/IMG/pdf/131108_Surveillance_mais_MON810_2012_Commentaires_CS_HCB.pdf

However, the specific analysis carried out by the HCB suggested a hypothesised increased tolerance of target pests in Spain when compared with the reference laboratory strain. This could be explained by, for example: (1) any type of change in the insecticidal Cry1Ab protein attributed to target pests (e.g. more or less toxic); (2) a modification (e.g. weakening) of the reference laboratory strain; and (3) an increased tolerance of the Spanish target pest populations to the Cry1Ab protein. The EFSA GMO Panel considered these three points.

Firstly, the EFSA GMO Panel noted that a new Cry1Ab toxin batch was used from 2012 onwards. In its PMEM report for the 2011 growing season of maize MON 810, Monsanto reported the outcomes of a bridging study[11] indicating that the old toxin batch, used until 2010, and the toxin batch, used from 2012 onwards, have similar biological activity on ECB.

Secondly, even though the 2012 dataset shows a trend towards increased MIC[12] values, it did not show any significant and consistent decrease in susceptibility of the ECB and MCB field populations in Spain.

The EFSA GMO Panel is of the opinion that the hypothesised increased tolerance of the Spanish target pest populations to the Cry1Ab toxin when compared with the reference laboratory strain, as suggested by the HCB, might instead be due to declining performance of the reference laboratory strain (e.g. infection with pathogens, inbreeding). In its 2012 PMEM report, the applicant also acknowledged that the reference laboratory strain might have shown poor performance but did not discuss the possible reasons for this. Such a statement should have been further elaborated by the applicant in its 2012 PMEM report. The EFSA GMO Panel therefore recommends that the applicant investigates the stability and quality of the reference laboratory strain.

In order to ensure an early detection of change in susceptibility of the ECB and MCB field populations, the EFSA GMO Panel strongly reiterates its previous recommendation for annual sampling of both target pests in areas of high maize MON 810 adoption rate, especially in north-east Spain in 2014 (see Table 1).

3.3. Further considerations on the harmonised IRM plan

As part of the harmonised IRM plan[13], the applicant proposed to sample multivoltine target pest populations every two years in areas where maize MON 810 adoption rate varies between 20 % and 80 % of the total maize cultivated area. Annual sampling is foreseen only in exceptional circumstances in areas of high uptake (i.e. > 80 % and therefore in areas where non-Bt refugia have not been implemented).

Based on the outcomes of the additional simulations with the Alstad and Andow (1995) model (see Appendix A of EFSA GMO Panel, 2013a), and considering that resistance evolution should focus on areas of high Bt maize adoption rates, the EFSA GMO Panel reiterates its previous recommendation that annual sampling of multivoltine target pests for maize MON 810 uptake between 50 % and 80 % of the total maize cultivated areas is put in place (see Table 1).

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[11] MON 810 2011 PMEM report, Appendix 8.
[12] Molting Inhibition Concentration (MIC).
[13] MON 810 2012 PMEM report, Appendix 6.

Table 1: Recommended sampling frequency of target pests

Maize MON 810 uptake[14] in a zone (% total maize cultivated area)	Sampling frequency	
	For a monovoltine target pest population	For a bi-/multi-voltine target pest population
< 20 %	None	None
20 % to < 50 % (R allele frequency of 3 %)	Biennial	Biennial
50–80 % (R allele frequency of 1 %)	Biennial	Annual
> 80 %[15]	Annual	

3.4. Farmer questionnaires

The EFSA GMO Panel, in close collaboration with the EFSA Unit for Assessment and Methodological Support (EFSA AMU Unit), assessed the methodology followed by the applicant to analyse the farmer questionnaires; and identified similar weaknesses as in previous PMEM reports.

Alongside the methodological guidance for a systematic evaluation of the farmer questionnaires, the evaluation of the overall 2012 farmer's survey (including, for example, sampling of farmers, types of questions, method of conduct interviews, data validation, method used for the design of the statistical analysis) is given in Appendix A.

Recommendations to the applicant for the improvement of the methodology are listed in Appendix A. However, from the analysis of the 2012 farmer questionnaires on maize MON 810, the EFSA GMO Panel concludes that no unanticipated adverse effects can be identified.

3.5. Literature review

The applicant identified 37 publications related to maize MON 810 and/or Cry1Ab protein (published between June 2012 and beginning June 2013). In addition, the EFSA GMO Panel identified a further five papers (Albajes et al., 2012; Daudu et al., 2012; Kamota et al., 2012; Raybould et al., 2012; Takacs et al., 2012).

Of all these publications, the EFSA GMO Panel identified only two publications (Albajes et al., 2012; Gu et al., 2013) that provide new information and were not assessed previously (for earlier assessment[16], see, for example, EFSA GMO Panel, 2012b, c, f, 2013a).

– Gu et al. (2013) reported a 97-day study on salmon (*Salmo salar* L.) with the initial body weight of 94 g with four different diets fed to triplicate pens, each with 100 salmon. Two basal diets were used: one free of soybean meal, and the other containing 15 % soybean meal. Each basal diet contained either 20 % maize MON 810 or its conventional counterpart. The diets were isonitrogenous and near iso-energetic. Zootechnical parameters were not influenced by the different diets. However, the whole body lipid content was significantly reduced in both MON 810 groups. The apparent protein and mineral digestibility (both lower in the soybean-containing diets) was decreased by MON 810 in both basal diets. No significant difference due to MON 810 in haematology and clinical chemistry was found. The relative weight of the whole intestine and the proximal intestine was significantly increased by MON 810 compared with its conventional counterpart after 33 days of feeding. However, the significance of this finding disappearing by the end of the study. Leucine aminopeptidase, used as a marker of enterocyte maturity, was reduced in the proximal intestine in both MON 810 groups,

[14] At the time of adoption of this opinion, maize MON 810 was the only Cry1-expressing maize cultivated in the EU. However, the EFSA GMO Panel recommends that in future the applicant takes into consideration the overall uptake of Cry1-expressing maize when identifying zones of high adoption for sampling target pests.

[15] In some regions where farmers do not comply with non-Bt refugia implementation.

[16] See also http://registerofquestions.efsa.europa.eu/roqFrontend/questionsListLoader?unit=GMO (with Question Number EFSA-Q-2014-00192).

compared with its conventional counterpart. Gamma-interferon (detected using real time quantitative polymerase chain reaction (qPCR)) in the distal intestine was significantly higher for MON 810 in the soybean-free basal diet. In conclusion, 20 % dietary MON 810 appears to have the potential to introduce immunogenic reactions in salmon of unknown consequences. It should be noted that the reported changes are the result of only about 2 % dietary protein. However, owing to the absence of non-GM commercial varieties, there is no measure of natural variation in the parameters measured. Consequently, it is not possible to conclude on the relevance of these findings in practice.

- Albajes et al. (2012) reported results from a Spanish study monitoring possible effects of maize MON 810 varieties on non-target organisms (i.e. predators as natural enemies). During the two-year study, the authors monitored the abundance of certain predators found in maize MON 810 fields compared with non-GM maize fields. The study did not show significant differences in predator densities except for rove beetles (i.e. *Staphylinidae*). A significantly higher number of rove beetles was found in one out of the two non-GM fields monitored. Compared with other non-target predators studied by Albajes et al. (2012), the overall number of rove beetles was very low. The authors also highlighted the fact that the effects on rove beetles are generally difficult to interpret because this family is heterogeneous in feeding habitats. Similar results had already been reported by de la Poza et al. (2005) and Balog et al. (2010). However, Garcia et al. (2010) indicated that the same rove beetle as monitored by Albajes et al. (2012) is not susceptible to Bt toxin. The authors also discussed the power of the statistical analysis of the field trials. Therefore, pending clear explanations for the aforementioned difference observed in rove beetles abundance, the authors concluded that further monitoring needs to be considered (e.g. susceptibility of rove beetles to Bt toxin, spatial and temporal exposure to maize MON 810/Cry1Ab toxin).

Consequently, in the light of the outcome of the two-year study by Albajes et al. (2012), the EFSA GMO Panel recommends that the applicant follows up possible adverse effects of maize MON 810 on rove beetles (e.g. through literature review).

4. Conclusions and recommendations

In its 2012 PMEM report, the applicant clearly states that the previously established methodologies were followed notwithstanding the EFSA GMO Panel recommendations to improve the methodology for PMEM of maize MON 810. The EFSA GMO Panel acknowledges that there was not enough time for the applicant to implement the latest EFSA recommendations (EFSA GMO Panel, 2013a). However, the EFSA GMO Panel also points out that its previous recommendations, as in its opinions on the 2009 and 2010 PMEM reports, have yet to be implemented (EFSA GMO Panel, 2011b, 2012a). Therefore, having already highlighted the poor sensitivity of the methodology[17] followed by the applicant, the EFSA GMO Panel reiterates all its recommendations (EFSA GMO Panel, 2011b, 2012a, 2013a) for consideration by the applicant in the PMEM plan and forthcoming PMEM reports.

Concerning the monitoring for changes in baseline susceptibility of target pests, the EFSA GMO Panel is of the opinion that the hypothesised increased tolerance of the Spanish target pest populations to the Cry1Ab toxin when compared with the reference laboratory strain, as suggested by the HCB, might instead be due to declining performance of the reference laboratory strain. The EFSA GMO Panel therefore recommends that the applicant investigates the stability and quality of the reference laboratory strain.

The EFSA GMO Panel concludes that the 2012 PMEM report did not show any significant and consistent decrease in susceptibility of the target pests field populations in Spain. However, in order to ensure an early detection of change in susceptibility of the ECB and MCB field populations, the EFSA GMO Panel strongly reiterates its previous recommendation for annual sampling of both target pests

[17] For further details, see also http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2012-00597

in areas of high maize MON 810 adoption rate, especially in north-east Spain in 2014 (EFSA GMO Panel, 2013a).

The EFSA GMO Panel further assessed two publications (Albajes et al., 2012; Gu et al., 2013) that provided new information and were not assessed previously. Consequently, the EFSA GMO Panel advises the applicant to follow up possible adverse effects of maize MON 810 on rove beetles (e.g. through literature review). In the publication by Gu et al. (2013), the authors reported local inflammatory responses in salmon fed maize MON 810. Currently it is not possible to conclude on the relevance of these findings in practice.

OVERALL CONCLUSIONS AND RECOMMENDATIONS

The data submitted by the applicant in its 2012 PMEM report do not indicate any adverse effects on human and animal health or the environment arising from maize MON 810 cultivation in 2012. However, the sensitivity of the methodology is still considered too low for an early detection of possible adverse effects. Therefore, the EFSA GMO Panel strongly reiterates all its previous recommendations for the improvement of the PMEM methodology of maize MON 810 (EFSA GMO Panel, 2011b, 2012a, 2013a).

In addition, the EFSA GMO Panel recommends that the applicant: (1) further investigates effects observed during the monitoring of baseline susceptibility of target pests in Spain; (2) follow-up possible adverse effects of maize MON 810 on rove beetles.

DOCUMENTATION PROVIDED TO EFSA

1. Letter from the European Commission, dated 4 March 2014, to the EFSA Executive Director requesting the assessment of the MON 810 monitoring report for the 2012 cultivation season provided by Monsanto; the 2012 PMEM report was annexed to the letter.

2. Comments from Member States on the PMEM report for cultivation of maize MON 810 in 2012.

3. Acknowledgement letter, dated 21 March 2014, from the EFSA Executive Director to the European Commission.

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APPENDIX

Appendix A. AMU technical report on the evaluation of farmer questionnaires

BACKGROUND

This Appendix A was prepared by the EFSA AMU Unit to support the EFSA GMO Panel in its evaluation of the PMEM report on maize MON 810 for the 2012 growing season, specifically to provide methodological guidance on evaluation of the farmer questionnaires submitted as part of the general surveillance (GS) programme, which aimed to identify adverse affects of the GM maize or its use on human and animal health or the environment that had not been anticipated in the ERA.

METHOD

Evaluation criteria were developed based on the principles of design for cross-sectional studies, and in particular surveys. The evaluation grid can be applied to surveys used for GS of GM plants. In July 2011, the EFSA GMO Panel updated its guidance on the PMEM of GM plants (EFSA GMO Panel, 2011a). The criteria reflect the recommendations in this guidance document. These criteria were previously applied in the assessment of the 2009 - 2011 MON 810 PMEM reports and the 2010 – 2011 Amflora PMEM reports (EFSA GMO Panel, 2011b, 2012 a,d,e).

Study design principle	Criteria
Sampling frame	1) The sampling frame used is specified 2) The total population included in the sampling frame is specified 3) The characteristics of the population included in the sampling frame are described, including region, agricultural practices, GM cultivation 4) The sampling frame coverage is appropriate for GM cultivation in the EU
Sampling method (sample bias)	1) The sampling method to select sample units from the sampling frame is described 2) The sampling method ensures sampling units from representative environments, reflecting the range and distribution of plant production systems and environments exposed to the GM plants and its cultivation are sampled 3) A list of sample units selected from the sample frame is provided 4) The sampling method minimises selection bias
Sample size (sample precision)	1) The size of the adverse effect to be measured is specified and scientifically justified and is within an acceptable limit of change. 2) The significance level is specified and the chosen level is scientifically justified (Type I error rate) 3) The power is specified and the chosen level is scientifically justified (Type II error rate) 4) A literature reference for the sample size method is provided 5) The sample size calculation method is appropriate for a proportion in a cross-sectional study 6) The sample size is sufficient to detect an adverse effect related to GM cultivation
Survey response rate (non response bias)	1) Follow-up method for non-responders is described and appropriate 2) Response rate is specified

	3) Details of losses in sampling are described 4) The number of partial responses and reasons for non-completion are specified 5) Comparison is made between characteristics of responder group and non-responder group 6) Comparison is made between characteristics of responder group and independent sources of information about the target population 7) The effects of non response bias have been minimised
Instrument design	1) The study design includes considerations to avoid interviewer bias 2) Where interviewers are used the interviewer training is described 3) The selection of open and closed questions is appropriate for the question type 4) The questions are clearly phrased and not open to misinterpretation 5) The questions encourage independent and objective responses 6) The comparator used in the study is described and appropriate for general surveillance 7) The instrument has been previously tested and validated
Instrument validity	1) Content validity – the survey includes questions relevant to assess • Background data Identifier of location of monitoring site and comparator site, surrounding landscape, type of field margins, proximity to conservation areas, cultivation and management of the GM field including recent history and previous cropping, soil (type, structure, quality), nutrient status, fertilization, irrigation. • Data informing on possible change in behaviour and performance of GMP Other GMPs cultivated, number of years of cultivation of GMP, cultivation and tillage from the removal of the previous crop to seed sowing, crop husbandry including sowing/planting date, post planting management, crop emergence, growth (vigour, height), pest, disease and weed management, flowering, standing ability, harvesting date and methods, yield, post-harvest management and subsequent cropping of the site, post-harvest storage, handling, processing, feeding • Data informing on possible ecological/environmental impacts of GMP on the protection goals and measurement Weed and pest populations, observations of other flora and fauna such as insects, birds and mammals, pollination and presence of pollinators, health of humans and performance of livestock. • Implementation of specific management requirements Implementation of risk management measures, coexistence segregation measures, stewardship recommendations, specific management due to regional environmental requirements 2) Criterion validity – agronomy parameters reported in the survey are compared with field trial data to test for concurrency 3) External consistency - results from survey are compared to and conform with independent external data sources (for example pest/weed occurrence reports, soil characteristics from geological surveys,

	authorisations and use reports for plant protection products) 4) Plausibility of responses – results for cultivation methods, agronomy parameters and weed/pest management practices reported in the survey conform to European agricultural practices 5) Construct validity – consistency and agreement between outcome variables is examined
Data validation	1) Data validation procedure are documented 2) Results excluded from the statistical analysis during validation are reported 3) Missing values are reported
Longitudinal aspects	Comparison with survey results from previous years 1) The survey is applied to the sample unit for multiple years in order to assess residual effects
Statistical analysis	1) Objective and hypotheses for analysis are clearly stated 2) A statistical analysis plan is provided 3) Statistical analysis includes analysis of pre-defined sub-groups according to PMEM guidance e.g country 4) Statistical analysis is appropriate for the data types 5) Results are clearly and consistently presented 6) The report should include descriptive statistics for the outcome variables 7) The issue of multiplicity is addressed 8) Methods for handling missing values are described 9) Where appropriate confidence intervals should be provided 10) The results of post-hoc analysis should be identifiable
Report conclusions	1) The report conclusions are clearly stated 2) The study design is appropriate to assess the conclusions 3) The data presented supports the conclusions presented in the report

RESULTS

Sampling frame

1) Sampling frame specification

Appendix 1 of the 2012 MON 810 report specifies that, in Portugal and Romania, the sampling frame for the survey was a public register. In Czech Republic and Slovakia, customer lists obtained from companies selling seeds were used. In Spain, the country with highest cultivation of maize MON 810 and therefore the largest number of surveyed farmers, no suitable sampling frame was available. As a consequence surveyors used previous contacts (the report states that '*the interviewers identify MON 810 cultivating farmers by knowledge from previous surveys or search in the region*').

2) Population included the sampling frame

Appendix 1 of the 2012 MON 810 report did not include information on the number of farmers in the sampling frame. The report states that '*the total number of farmers cultivating MON 810 per country is not known*'. However, it is indicated that '*In the moment, only the total cultivated area (in ha) is known instead of the total number of growers (and of fields and field sizes). That implies that the sampling frame for this survey can not be based on the whole of fields with MON 810 cultivation in Europe. Therefore a quota considering the area of cultivation (ratio of country and total area) will be the first subdivision factor. Additionally, the product situation (and therefore the field sizes) within the countries serves for the second subdivision factor. Both subdivision factors result in the number of farmers to be monitored per year and country.*'

3) Characteristics of the population included in the sampling frame

Appendix 1 of the 2012 MON 810 report did not include information on the characteristics of the farmers included in the sampling frame. Information on the number of farmers in the sampling frame according to country, region, agricultural practices, size of farm/number of fields and previous cultivation of GM crops is important.

4) Sampling frame coverage

Information on the sampling frame was not provided in Appendix 1 of the 2012 MON 810 report, and therefore this is difficult to assess. The report states that *'The customer lists of the seed selling companies do not completely cover all MON 810 cultivating farmers, so that some are missing'* but does not try to characterise the missing farmers. Table 3.2 indicates that farmers from all the countries growing maize MON 810 were included in the survey. The percentage of maize MON 810-planted surfaces surveyed ranged between 3.3 % in Spain to 99.5 % in Romania. For Europe as a whole, 7.1 % of maize MON 810-planted surfaces were surveyed – this is a decrease from 12.5 % in 2009, 13.3 % in 2010 and 9.9 % in 2011. In fact, in 2012 a decrease in the number of hectars (ha) of monitored planted MON 810 surfaces was observed in comparison to 2011 (9118 in 2012 vs. 11330 in 2011). Since the survey size per year is fixed at 250 farmers and the area of maize MON 810 cultivation has increased this proportion may continue to decrease. Full details on the source of the sampling frame, the number of farmers and the major characteristics of the farmers should be included in the survey report. The national registers set by Member States on the cultivation of GM crops would be the optimum sampling frame, however the PMEM report notes that, when using public registers, they *´do not necessarily contain the contact data of the farms so it is often very difficult to identify them.´* Both in cases of incomplete customer lists of the seed selling companies and of incomplete contact data in public registers, it needs to be considered whether the data might be missing systematically.

Sampling method

1) Selection of sample units

Appendix 1 of the 2012 MON 810 report states public registers and customer lists of the seed selling companies have been used as sampling frames in 2012, but in one country no sampling frame was available. For this country, the report states that '*the interviewers identify MON 810 cultivating farmers by knowledge from previous surveys or search in the region.'* Survey design methodology requires the sampling frame to be representative for the target population, in this case European farmers growing MON 810, and that the random selection process is applied to the sample units in the sampling frame prior to proceeding with the interviews. A description of the method to ensure that units are randomly selected from the sampling frame should be included in the report, including where relevant the statistical software and/or the program code used for this procedure.

2) Sampling of units from representative environments

Appendix 1 of the 2012 MON 810 report states *'Sampling of these 2500 fields should ensure to reflect the range and distribution of plant production systems and environments exposed to the GM plant and its cultivation. This range, on the one hand, is characterised by the growing season (year and its climatic, environmental conditions). On the other hand, it is characterised by the regions where GM cultivation takes place. Regions may be various production systems, regulatory requirements, agro-political and socio-economic conditions and can therefore be best described by European countries. Sampling therefore takes place within strata (defined by years and countries of cultivation)'*. It is also further stated that: '*Subdividing the number per year into the cultivation regions considers fluctuant adoption of the GM plant (grade of market maturity) and therefore is performed yearly for the actual situation*' and that: '*Consequently, cultivation areas with a high uptake of the GM plant will be over-represented by a high number of fields to be monitored. Within each stratum (per year and country) the determined number of monitoring units is selected randomly where each field has the same chance* *to be surveyed. The whole sampling procedure ensures that the monitoring area will be proportional to and representative of the total regional area under GM cultivation.'*

This differs from the 2011 MON 810 report, which stated: *´two strategies for selecting farmers are applied: in MS with a high rate of market penetration a certain number of farms will be selected whereas in MS with low cultivation rates preferably all MON 810 cultivating farmers are interviewed´* and from the 2010 MON 810 report which stated: *´For selecting farmers in countries with higher market penetration a procedure is applied to select: at least 10 % of farmers and 10 % GM area per region and at least 20 % of new farmers each year´*. To ensure units are selected from representative environments (regions with high uptake of maize MON 810), a proportion of farmers to be selected from each strata (e.g. country) should be clearly defined and consistently applied in each year of the survey. It is described that the number of farmers to be monitored per year and country is determined based on two subdivision factors (mentioned above) but it is not entirely clear how this is done. For example, based on table 3.2, Spain seems to have 90.1 % of the total European planted MON 810 surfaces but contributing only about 70.3 % of the questionnaires for 2012. Moreover, the claim that each field within a stratum has the same chance to be surveyed is not entirely substantiated, since sampling selection considers farmers and not fields and also it is stated that: '*In the moment, only the total cultivated area (in ha) is known instead of the total number of growers (and of fields and field sizes). That implies that the sampling frame for this survey can not be based on the whole of fields with MON 810 cultivation in Europe.*'

3) Proportion of sample units selected

The number of farmers surveyed in each country is provided, but no indication of the total number of farmers in each country and region included in the sampling frame is given. Table 3.2 describes the proportion of maize MON 810-planted area covered in the survey. Information on the farmers included in the sampling frame and selected from the sampling frame should be provided as evidence that the sampling method has been successfully implemented.

4) Selection bias

If the number of farmers cultivating maize MON 810 increases, it will be difficult to ensure all farmers within a region are interviewed and, as a consequence, an appropriate sampling methodology becomes more important. The report provides limited information on the sampling methodology and the possibility of selection bias and achievement of inadequate power in the survey cannot be excluded. The grouping of sample units according to the strata and random selection of sample units from within the strata should be performed using the specified sampling frame prior to conducting the interviews. A description of the method to ensure that units are randomly selected from the sampling frame should be included in the report, including where relevant the statistical software and/or the program code used for this procedure. The proportion of new farmers and farmers with previous experience of maize MON 810 selected from the sampling frame for each region should be presented in the report to provide evidence that the sampling method ensures that areas of intensive maize MON 810 cultivation are appropriately covered in the survey. If the used sampling frames (public registers and customer lists obtained from companies selling seeds) were missing information in a systematic way (i.e. specific subsections of the farmers' populations) then bias could be introduced in the study if the reasons for the missing information would be related to the study outcomes. Moreover, in the case of Spain, where no suitable sampling frame was available, it was noted that: '*Here, the interviewers identify MON 810 cultivating farmers by knowledge from previous surveys or search in the region.*' This approach cannot guarantee a representative sample, and therefore, it has a possibility of introducing bias (the direction of which cannot be predicted). It is not explained how exactly this selection is done, however, it is possible that it might make it more likely to sample some of the same farmers in consecutive years, perpetuating a possible bias, in case some bias existed in the first place.

Sample size

1) Size of the adverse effect

Appendix 1 of the 2012 MON 810 report states that the null hypothesis is that the proportion of responses that are not ´as usual´ is equal to or above 10 %. Therefore, the threshold or margin for adverse effects is 10 % (i.e. 5 % above the baseline). No specific reference from the scientific literature was provided to support the selection of 10 %; however, for this type of study 10 % represents an acceptable limit of change. A 10 % effect size has also been selected in a framework proposal for post-release monitoring of second-generation crops with novel traits in Canada (Beckie et al., 2010).

2) Type I error rate

The type I error rate is $\alpha = 0.01$ in Appendix 1 of the 2012 MON 810 report. This denotes that there is a 1 % probability of rejecting the null hypothesis that there is a 'proportion of adverse effects equal to or greater than 10 %' when it is true, i.e. failure to detect a true adverse effect. A type I error rate of 1 % is conservative and acceptable. It needs to be noted that the error rates are specified for each one-sided test, separately, but it is not clear what these error probabilities would be if both tests (for each question) were considered together.

3) Type II error rate

The type II error rate is $\beta = 0.01$ in Appendix 1. This denotes that there is a 1 % probability of not rejecting the null hypothesis that there is a 'proportion of adverse effects equal to or greater than 10 %' when it is false, i.e. falsely detecting an adverse effect. The selection of 0.01 will result in a large sample size. However, it needs to be noted that this error rate will be realised only with the overall calculated sample size of 2500. For a yearly survey, as calculated in section 2.6, for a real proportion of 5 % of a plus or minus answer, a sample size of 250 and an α of 0.01 the power to detect 'no effect' would be 73 %, i.e. the type II error rate, β, would be 0.27.

4) Reference for the sample size method

The sample size calculation was performed using the methodology described in Rasch et al. (2007).

5) Sample size calculation

The sample size is calculated assuming difference testing.

6) Sample size

As concluded for the 2011 PMEM report, the selection of parameters for the sample size calculation is conservative. In 2012, 249 farmers were sampled – this is one farmer less than the planned 250 farmers per year. Nonetheless, it is likely that the same farmer may be surveyed in different years and therefore sample units may not be independent from each other. Consideration of this factor should be included in the sample size calculation. Most importantly, the power of the study will be achieved only when the sample size of 2500 farmers/fields surveyed is achieved after 10 years. Concerning the 'allocation' of the calculated sample size among the participating countries, it is described that the number of farmers to be monitored per year and country is determined based on two subdivision factors (mentioned above) but it is not entirely clear how this is done.

Survey response rate

1) Follow-up for non-responders

Appendix 1 of the 2012 MON 810 report states ´*The surveys are performed after the planting season, the farmers are provided with a copy of the questionnaire at least two weeks before a telephone interview or interviewed face-to-face.*´ This should reduce the number of non-responders in comparison with other survey methods. No information is provided in the report on the follow-up for non-responders.

2) Response rate

The response rate is provided (95.7 % for Czech Republic and 100 % for Spain, Portugal, Slovakia and Romania). In Appendix 1 of the 2012 MON 810 report, the fact that one farmer from the Czech Republic refused to participate is recorded.

3) Losses in sampling

No details of losses in sampling are included in the report. The number of farmers selected from the sampling frame but not contacted by the interviewers should be stated in the report.

4) Partial responses and reasons for non-completion

This information was not presented in the report. However, the use of trained interviewers may have resulted in no cases of partial completion of the survey.

5) Characteristics of responder group and non-responder group

One farmer from the Czech Republic declined to participate. It is important to know if a specific subgroup of farmers is not participating in the survey and therefore is not represented in the survey findings; consequently, this comparison should be presented in the report.

6) Characteristics of responder group compared with the target population

No comparison between the responder group and the target population is provided in the report. Where available, national registers for the cultivation of GM crops should be compared with the characteristics of the farmers surveyed in terms of geographical location and farming practices to ensure that the farmers surveyed are representative of the target population.

7) Non response bias

The losses to sampling should be fully documented in the report to provide evidence that there is no non-response bias. It is important to know if a specific subgroup of farmers is not participating in the survey and therefore is not represented in the survey findings.

Instrument design

1) Interviewer bias

The 2012 MON 810 survey used third parties to perform the interviews, with the exception of Romania, where Monsanto field representatives assisted the farmers to fill in the questionnaire. The use of third-party interviewers can prevent interviewer bias. A lot of attention should be paid to the standardisation of the delivery of the questions from all interviewers, since the interviews should be conducted in the same way for all participants. This means also that the administration of the questionnaire should be done in the same way for all participants; in 2012, some interviews were done during personal visits, while others were done by telephone communication (in which case the farmers were getting the questionnaire two weeks in advance).

2) Interviewer training

Appendix 1 states that *‘all interviewers have been trained to understand the background of the questions’*, and mentions that the interviewers also draw on previous experience in administering the questionnaire to ensure that the questions are completed correctly. In addition, a ´user’s manual´ is provided to the interviewers.

3) Question type

The questionnaire contains 27 closed questions, which require a comparison between the representative GM maize field and the representative conventional maize field. For these questions the response options are “´the same´ or ´different/changed´ ” or “ ´as usual´ or ´worse´ or ´better´ ”. It is these questions that are primarily analysed in the report. Where the response is not ´same/as usual´, there is an option to provide more details as free text. There is also a mix of closed and open questions to gather additional information about the farming practices on the farm and five closed questions to gather information about good agricultural practice and implementation of non-Bt refuge(s). The combination of open and closed questions allows quantitative analysis of the comparisons between the GM maize field and the conventional maize field, and, where differences occur between the two field types, explanatory analysis can be performed using the information from the free text questions.

4) Phrasing of questions

The questionnaire uses questions based on farm records and should be understood by a grower.

5) Independent and objective responses

Overall, the questionnaire seeks to obtain an objective set of responses to summarise the results and experiences during the growing season for maize. Nevertheless, the questionnaire could be improved by adjusting the balance between crop performance questions and questions on the general farm environment by addressing the latter more fully. Furthermore, qualitative responses may sometimes relate to a subjective assessment on the part of the farmer. An effort should be made to use objective measurable outcomes, whenever this is possible.

6) Comparator

The questionnaire relies on a comparison between a representative GM maize field and a representative conventional maize field in order to detect unanticipated adverse effects. Consequently, the choice of representative fields and the recollection of similarities and differences are crucial to the success of the survey. The report provides no indication about the comparator fields selected by the farmer for comparison in the survey, however Figure 3.3 of mean percent of maize MON 810 cultivation area of total maize area per farmer appears to indicate that on all farms some non-GM maize is grown that may be suitable as a comparator. It is recommended that the questionnaire contains questions to record clearly whether the comparator field is growing on the same farm at the same growing season and the variety of the comparator. If no comparators are being grown spatially or temporally close to the GM crop, then the rationale for selecting another comparator (e.g. maize grown in previous years) should be fully described. The comparators selected by the farmers for the survey should be summarised in the PMEM report.

7) Validation of the instrument

The questionnaire was developed by the German Federal Biological Research Centre for Agriculture and Forestry and maize breeders and statisticians in Germany, and the results of the pilot of this questionnaire were published in 2004 (Wilhelm et al., 2004). The questionnaire was used in annual PMEM reports in the period 2006–2012. Any future amendments to the questions should be made giving consideration to pooled analysis of the results over 10 years. The report mentions: ‘*The format* *of the questionnaire is reviewed on a yearly basis based on the outcome of the latest survey. As appropriate, adjustments are made to improve the statistical relevance of the collected data*'. As a consequence of this approach, increased care should be taken to assure the comparability of the obtained data from year to year.

Instrument validity

1) Content validity

- Background data

Background data relating to geographical location at country and county level, surrounding environment, soil type, crop rotations in the previous 2 years and fertiliser treatments and irrigation are collected by the questionnaire. It would be of value to take longitude and latitude measurements of the representative GM maize field; information of this nature would facilitate linkage with other spatial monitoring datasets. In addition, the questionnaire should record for how many years the farmer has been growing maize MON 810 on the farm, and the question on crop rotation should also record, for rotations in which maize was grown, whether this was GM or conventional maize.

- Data informing on possible change in behaviour and performance of the GM crop

The following characteristics were monitored to obtain data on any change in the behaviour and performance of maize MON 810: crop rotation, time of planting, tillage and planting technique, insect control practices, weed control practices, fungal control practices, fertiliser application, irrigation practice, time of harvest, germination vigour, time to emergence, time to male flowering, plant growth and development, incidence of stalk/root lodging, time to maturity, and yield. It is noted that information on plant protection products applied to the GM maize field was collected, but the same information was not supplied for the conventional field. In order to fully explain changes in plant protection product use, the products applied to the conventional field should also be recorded, and the quantities applied over the season to the GM maize field and the comparator field should be recorded.

- Data informing on possible ecological/environmental impacts of the GM crop on the protection goals and measurement

The following characteristics were monitored to obtain information on possible ecological/environmental impacts of maize MON 810 on protection goals: occurrence of MON 810 volunteers, disease susceptibility, insect pest control (*O. nubilalis*), insect pest control (*Sesamia* spp.), pest susceptibility, weed pressure, occurrence of insects, occurrence of birds, occurrence of mammals. For the closed questions on occurrence of insects, birds and mammals, the option ´*Do not know*´ is included; however, it has been excluded in other closed analysis questions, forcing the farmer to make a clear assessment. Allergenicity in people handling the GM crop during production and harvesting could be an adverse effect: a question to assess this should be included in the questionnaire. It is important that the question is phrased in such a way that it discriminates between allergenicity to the GM crop and background levels of hay fever type symptoms.

- Compliance with good agricultural practice

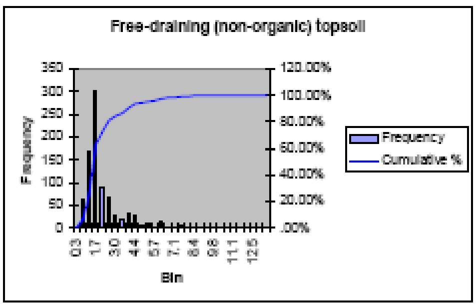
Section 4 requests information on compliance with good agricultural practice, and in this case the planting of non-Bt refuge(s).

2) Criterion validity

The scientific opinion of the EFSA GMO Panel on the renewal of the authorisation for maize MON 810 commercialisation in the EU (EFSA, 2009) states that ´*The information available in the renewal applications gives no reason to change the opinion that maize MON 810 is agronomically and* *phenotypically equivalent to currently grown non-GM maize varieties, with exception of the insect resistance conferred by the Cry1Ab protein.´* The 2005 scientific opinion for maize MON 863 × MON 810 × NK603 (EFSA, 2005) states *´Plants of the same field trials as for compositional analysis, except for a difference in glyphosate treatment (see section 3.2.2) were compared for their agronomic and phenotypic characteristics. These characteristics included seedling vigour, crop growth stages (for example, the stage at which silking and pollination occurred), height of the plant and ear (attachment containing the cob and kernels), root lodging (plants leaning to the surface), stalk lodging (plants with stalks broken below the ear), dropped ears, final stand count, stay-green and kernel yield. The plants tested showed no particular deviations in any of these parameters. In addition, plant damage due to insect feeding in two locations and due to weather in one location appeared to occur preferentially in plots planted with reference lines.´* Report MSL-18567 (Carringer et al., 2004) includes data on the agronomic parameters assessed in the above opinion. In the case of seedling vigour, both maize MON 810 and the reference varieties had ´excellent´ vigour, with the exception of one site where one reference variety was classed as poor and one as average. Stalk lodging in plants near harvest was observed more frequently in the reference varieties, and at one site root lodging in plants close to harvest was observed more frequently in the reference varieties. In the case of the other agronomic parameters, there was no particular deviation between maize MON 810 and the reference varieties. Appendix 1 of the 2012 MON 810 report assessing the characteristics of maize MON 810 reported ´unchanged germination vigour, unchanged time to emergence, unchanged time to male flowering, unchanged plant growth and development, lower incidence of stalk/root lodging, delayed time to maturity, higher yield and unchanged occurrence of MON 810 volunteers.´ Comparing the field trial data with the farmer survey data provides an opportunity to check the validity of the farmers' responses. It appears that there may be differences between field trial data and the questionnaire: there are a number of possible explanations for this, e.g. the conventional crops grown on the farms differ from the comparator variety used in the field trials, the information provided by the farmers is biased or erroneous or the GM crop is performing differently on farm-scale cultivation (possibly performing better when the cultivation conditions are less than optimal). It is of value to select parameters measured using a ´gold standard´ methodology and to contrast these with the responses in the survey to ensure the validity of the reported responses.

3) External consistency

Comparison of the data reported in the survey with information from independent data sources provides a further opportunity to test the validity of the responses. The information on soil quality offers the opportunity to compare it with the information held in the Soil Profile Analytical Database for Europe (SPADE-2) (Hollis et al., 2006). Figure 1 shows the information on top soil organic carbon contained in this database. The MON 810 survey reports organic carbon content values between 0.6 % and 5.9 % with a mean of 1.8 %. It can be seen that this range falls within that of the SPADE-2 range for organic carbon content. It should be noted that the SPADE-2 database provides a useful dataset for European soil properties but that the values are based on a limited set of soil samples for each EU country.



Mean	1.983665
Standard Error	0.051215
Median	1.5
Mode	1.5
Standard Deviation	1.494919
Sample Variance	2.234783
Kurtosis	9.998333
Skewness	2.648682
Range	13.1
Minimum	0.3
Maximum	13.4
Sum	1690.082
Count	852
Confidence Level(95.0%)	0.100523

Figure 1: Distribution and descriptive statistics of top soil organic carbon contents in SPADE-2 forfree-draining non-organic soils.

4) Plausibility of responses

The report states that: '*All data are entered and controlled for their quality and plausibility. A quality control check first checks the completeness of the data. Some data fields (especially the monitoring characters or comments in case of farmer's assessments differ from As usual) are defined to be obligatory, therefore missing values or unreadable entries are not accepted. Furthermore the values are checked for correctness (quantitative values within a plausible min-max range, qualitative values meeting only acceptable parameter values). Plausibility control checks the variable values for their contents, both to find incorrect answers and to prove the logical connections between different questions. It also looks for the consistency between Plus/Minus-answers and specifications, i.e. whether all these answers were provided with a specification and whether the specifications really substantiated the Plus/Minus-answers*'.

It is indicated that the sowing and harvest times were used to check the plausibility of the responses provided by the farmers: the sowing time ranged from 1 March 2012 to 7 July 2012 and the harvest time for maize grain ranged from 15 August 2012 to 30 December 2012 and for maize forage from 20 August 2012 to 30 October 2012.

5) Construct validity

The questionnaire is able to detect changes in characteristics of the GM maize field compared with the conventional field that could be predicted when the nature of the genetic event in MON 810 is considered. Maize MON 810 expresses the *cry1Ab* coding sequence, which encodes an insecticidal protein, Cry1Ab. The responses to the survey indicated that, for the maize MON 810 field, insecticide application and corn borer control practices were different: owing to a reduction in insecticides applied to control corn borers, the yield was higher, there was a lower incidence of root and stalk lodging and less susceptibility to diseases and pests. The questionnaire also indicated that the control of ECB and pink borer in maize MON 810 fields was very good. The report proposes that the change in previously mentioned characteristics is due to the increased protection from corn borer damage. This hypothesis is credible and indicates consistency and agreement among outcome variables.

Data validation

1) Validation procedures

Section 2.7 of Appendix 1 describes the data management and quality control procedures. It states that '*For not readable entries in the questionnaires, queries were formulated and the field representatives or farmers were asked for clarification. These entries in the database were corrected*'. In section 3.1 it is further explained that '*After the first quality and plausibility control, 27 farmers were contacted again to provide additional clarifications (10 from Romania, 6 from Spain, 6 from Portugal and 5 from Czech Republic). Examples of items that had to be clarified were incorrect variety names (MON 810 varieties as well as conventional varieties) and missed answers (surrounding environment, soil quality, weed and pest control practices in conventional maize as well as in MON 810, date of harvest, application of fertilizer and weed pressure in MON 810). Several farmers were also asked to clarify some inconsistencies between weed and pest control practices in conventional maize compared to MON 810, and plant protection products used in MON 810. Furthermore, discrepancies between named conventional varieties and planting of a refuge had to be resolved. After including the corrections, the quality and plausibility control confirmed that all 249 questionnaires could be considered for analysis*'. In this report, the number of questionnaires that require further clarification with the farmers is included, however, a classification by error types should also be presented.

2) Exclusion of results

All completed questionnaires (249) were included in the analysis.

3) Missing values

It is stated in the report: '*When farmers gave no statement, these answers are accounted as missing values and therefore not considered valid'*. There are several questions for which the number of valid answers was less than 249. In the analysis of each of the monitoring characteristics, the number of responses for each value was shown in the table, including the missing values where they occur. In general, the missing values were few.

Longitudinal aspects

1) Sampling over multiple years

The repeated sampling of a sample unit needs to be considered in the sample size calculations and in the statistical analysis of the results. It is important that a mechanism for recording repeated sampling is introduced and the numbers of sample units repeatedly sampled are included in the report. If this information were available, it would allow an analysis considering the intensity of maize MON 810 cultivation and the possible changes in monitoring characteristic assessment as maize MON 810 cultivation is repeated in consecutive years.

Statistical analysis

1) Objective and hypotheses

Appendix 1 states: '*The aim of the survey is to identify potential adverse effects that might be related to MON 810 plants and their cultivation. For that reason, most questions are formulated to get ordinary data, i.e. with three possible answers (Plus/ As usual/ Minus). The Plus- and Minus-answers indicate a deviation from the situation with conventional maize and are provided with a specification to describe the specific effect and its potential cause. High frequency (> 10 %) of Plus or Minus-answers would indicate possible effects*'.

2) Statistical analysis plan

Section 2.4 of Appendix 1 describes the statistical test procedure. The effect is defined as: '*An effect of the cultivation of MON 810 or any other influencing factor would arise in a greater percentage of Plus or Minus answers, where "greater" or an effect, was quantitatively defined by exceeding a threshold of 10%*' It would be expedient to provide scientific references to support the selection of the 10 % threshold. Additionally, for certain responses, 10 % may be greater than the acceptable limit of change. Alternative statistical analyses allowing the exploration of different effect sizes for certain monitoring characteristics would assist in the interpretation of the results. The null hypothesis is that the proportion of responses not ´as usual´ is equal to or above 10 %. A significance level of 0.01 % was used in the statistical test. If $p < 0.01$, then the null hypothesis that the minus/plus response is equal to or greater than 10 % is rejected and therefore no effect can be identified.

3) Pre-defined subgroups

The analysis was performed for all fields surveyed in 2012. There was no analysis of country level data. Given the number of farmers surveyed in some countries, analyses of country-level subgroup may not have been statistically valid; however, consideration should be given to the fact that Member States may require country-level results. Moreover, in the report it is mentioned: '*Sampling therefore takes place within strata (defined by years and countries of cultivation)*'. This stratified sampling should also be taken into consideration in the statistical analysis, which currently considers the sample as 'homogeneous' being comprised of independent units (farmers). In addition, analysis of the assessment of monitoring characteristics by new farmers compared with farmers with previous experience of cultivation of maize MON 810 would be of interest. This could assist in detecting residual effects.

4) Statistical analysis

The reports states that plus responses and minus responses were ´statistically tested by using the exact binomial test´. This test is appropriate for the ´same/different´ type of question. However, for questions of the ´as usual or worse or better´ type, where there are three outcomes, an analysis using a multinomial test should be performed (in this case a trinomial test). Galyean and Wester (2010) used simulation methods to generate experimental count data from multinomial distributions in order to compare multinomial and binomial proportion methods for analysis. It was concluded that analysing multinomial data as a series of binomial proportions increased the survey-wise type I error rate and recommended to use a multinomial analysis to test for the distributional difference with a subsequent binomial approach used to test for differences in a specific category or to correct for the multiplicity of testing.

5) Results presentation

For each monitoring characteristic measured by the survey, a table of the responses was provided with percentage and ´valid percentages´ (the proportion of answers excluding missing values) plus, often, a bar chart of the frequency of responses. The valid percentages were used in the binomial test. The reasoning between the valid percentages in the table of responses and the table of the results of the binomial test for different ´treatments/practices´ should be further explained by the applicant in order to facilitate interpretation of the results. Moreover, the presentation of a power calculation in situations in which the null hypothesis has been rejected is not necessary.

6) Descriptive statistics

Descriptive statistics were provided for the continuous outcome values number of fields, maize area in hectares, percentage humus content, sowing date and harvest date. The analysis of the categorical values was provided as frequency tables.

7) Multiplicity

A significance level of 0.01 was used, but the issue of multiplicity of testing was not addressed. Another major problem is related to the fact that the analysis needs to be pooled after 10 years to achieve the statistical power described in the sample size calculations. Each annual report represents an interim analysis, and the statistical analysis plan needs to compensate for these interim analyses, considering also possible situations in which the same farmer(s) is (are) sampled in more than one years.

8) Handing missing values

In the tables two percentages were presented: the ´Percent´, which included missing values, and the ´Valid percentages´, in which the missing data or the ´Don't know´ responses were excluded.

9) Confidence intervals

For statistical tests it is standard practice to use confidence intervals, and these were not usually included in Appendix 1. In the table summarising the analysis of the monitoring characteristics (e.g. Table 3.1 in Appendix 1) the confidence intervals should be included. The inclusion of confidence intervals would allow an understanding of the sensitivity of the analysis to the choice threshold.

10) Post-hoc analysis

Post-hoc analysis was performed only in situations in which an effect was identified and further explanatory analysis was possible using less structured information, e.g. free text collected in the questionnaire.

Report conclusions

1) Report conclusions

Appendix 1 contains the following conclusions:

‘*2012 data indicates that in comparison to conventional maize plants, MON 810 plants*

• received less insecticides caused by their inherent protection against certain lepidopteran pests,

• had less incidence of stalk/root lodging caused by the inherent protection against certain lepidopteran pests,

• had a longer time to maturity caused by the absence of pest pressure of certain lepidopteran

pests,

• gave a higher yield caused by the better fitness of the plant,

• were less susceptible to diseases caused by hardly any insect feeding damage,

• controlled corn borers very well caused by the inherent protection against certain lepidopteran

pests, and

• were less susceptible to pests, other than corn borers, especially lepidopteran pests caused

by the inherent protection against certain lepidopteran pests and the resulting better fitness

of the plants’.

2) Study design

The study design was appropriate to evaluate whether a set of monitoring characteristics relating to plant performance and management practices for maize MON 810 cultivation in the current year of the survey differed from a comparator variety by a threshold of 10 %. However there are indications of weaknesses in the sampling methodology applied for the survey and as a consequence the possibility of selection bias in the survey cannot be excluded. In addition the result of this assessment was very much dependent on the selection of an appropriate comparator.

Certain effects may reach a sufficient magnitude for detection only with repeated cultivation of a GM crop, and so amendments to study design and the analysis plan should be considered in order to assess the effect of multiple years of GM crop cultivation. Tables 4.1 and 4.2 in Appendix 1 present the results from the previous six years and the 2012 results. The inclusion of the pooled results would be of interest.

3) Substantiation of results

Fourty-three farmers (17.3 %) indicated that they had changed their insect control practices in the maize MON 810 compared to conventional maize in 2012; The report states: ‘*The difference arises from farmers using less insecticide applications in general’* and *‘as well as from farmers not controlling corn borers any more with conventional insecticide applications*’. Seventy farmers (28.1 %) reported a reduction in stalk and root lodging in the maize MON 810 compared with the conventional field. A reduction in stalk and root lodging was also observed in the field trial studies. Concerning ‘time to maturity’ there is some inconsistency between the number of farmers reporting a delayed time to maturity mentioned in the text (32 farmers) and in the tables (40 farmers). The respective statistical test in based on fourty farmers (16.1 %) reporting delayed maturity. Forty-three farmers (17.3 %) reported that the maize MON 810 field was less susceptible to diseases, with associated reports of reduced susceptibility predominantly to *Fusarium* spp. (21 farmers) and *Ustilago maydis* (18 farmers). The reports of reduced susceptibility to fungal infections were substantiated with similar findings from the scientific literature. Two hundred and twenty-four farmers (valid percentage: 91.1 %) and 196 farmers (valid percentage 90.7 %) reported that maize MON 810 provided ´very good´ control of ECB and pink borer, respectively. These results are to be expected, as the genetic modification provides protection from corn borers and therefore should result in a healthier crop. Fifty-three farmers (21.3 %) reported maize MON 810 to be less susceptible to pests other than the the two borers mentioned above (with associated reports of reduced susceptibility predominantly to pests of the orders Lepidoptera and Arachnida). An increased yield was reported by 107 farmers (43 %); as maize MON 810 has less insect damage, an increased yield is not unexpected.

For the monitoring characteristics above, the null hypothesis that an effect was evident could not be rejected. One farmer (0.4 %) reported an assessment of the MON 810 maize as more susceptible to pests other than the the two borers mentioned above (ECB and pink borer) compared to conventional maize (however, the corresponding null hypothesis of $f_{\text{more susceptible}} \geq 0.1$ could be rejected). while a lower yield, in comparison with conventional maize, was reported by 6 farmers (2.4 % - however, the corresponding null hypothesis of $f_{\text{lower}} \geq 0.1$ could be rejected). Presenting all results with confidence intervals would have facilitated the interpretation of the results and would have allowed the effect of the selection of alternative threshold values other than the arbitrarily selected 10 % to be explored.

The monitoring characteristics that were not *´as usual´* described above were also observed in the 2011 PMEM reports. In 2012, not *´as usual´* responses above the 10 % threshold related to the occurrence of volunteers were not observed. The consistency of the results in each year of survey indicates the stability of the observed effects. Interpretation of the results should be viewed with caution as there are indications of weaknesses in the sampling methodology applied for the survey and as a consequence the possibility of selection bias in the survey cannot be excluded. It is important that an appropriate and consistent sampling methodology is used. The grouping of sample units according to the strata and random selection of sample units from within the strata should be performed using the specified sampling frame prior to conducting the interviews. A description of the method to ensure that units are randomly selected from the sampling frame should be included in the report, including, where relevant, the statistical software and/or the program code used for this procedure. The proportion of new farmers and farmers with previous experience of maize MON 810 selected from the sampling frame for each region should be presented in the report to provide evidence that the sampling method ensures that areas of intensive maize MON 810 cultivation are appropriately covered in the survey.

Recommendations and Conclusions

From the data provided in the 2012 farmer’s survey to monitor adverse effects associated with the cultivation of maize MON 810, no adverse effect can be identified. However the 2012 report provides limited information on the sampling methodology and the possibility of selection bias in the survey cannot be excluded. Therefore, the following improvements to the survey design and reporting are recommended:

- Full details on the source of the sampling frame, the number of farmers and the major characteristics (e.g. previous cultivation of maize MON 810) of the farmers should be included in the survey report. The national registers set by Member States for the cultivation of GM crops would be the optimum sampling frame, if available.

- A full description of the method by which the number of farmers to be monitored per year and country is determined, should be provided. It is currently, indicated that this is based on two subdivision factors, however, inadequate clarification is given on how this is actually done.

- A description of the method to ensure that units are randomly selected from the sampling frame should be included in the report, including, where relevant, the statistical software and/or the program code used for this procedure. The proportion of new farmers and farmers with previous experience of maize MON 810 selected from the sampling frame for each region should be presented in the monitoring report to provide evidence that the sampling method ensures that areas of intensive maize MON 810 cultivation are appropriately covered by the survey.

- The losses to sampling should be fully documented in the report to provide evidence that there is no non-response bias. It is important to know if a specific subgroup of farmers is not participating in the survey and therefore is not represented in the survey findings;

- It is recommended that independent trained interviewers are used to reduce interviewer bias. It is also recommended that the interviews are conducted in the same way for all participating farmers, for example either by telephone or by personal interview. In cases that this is not possible, additional attention should be given to the uniformity of the delivery of the questions and the achievement of results of comparable quality.

- It is recommended that the farmer questionnaire contains questions to record whether the comparator field is growing on the same farm in the same growing season and the variety of the comparator. If no comparators are being grown spatially or temporally close to the GM crop, then the rationale for selecting another comparator (e.g. maize grown in previous years) should be fully described. The comparators selected by the farmers for the survey should be summarised in the PMEM report.

- Farmer questionnaires should focus only on changes that would be recognised by the farmer during the daily management of the farm. However, additional questions could be included to gain a better understanding of the intensity of GM maize cultivation on the farm (number of years of maize MON 810 cultivation and frequency of maize MON 810 in crop rotations), and further information on plant protection product usage (in particular, in the comparator field) should be obtained to facilitate a full understanding of any observed changes. Moreover, qualitative responses may sometimes relate to a subjective assessment on the part of the farmer. An effort should be made to use objective measurable outcomes, whenever this is possible.

- Confidence intervals for the analysis of the monitoring characteristics should be included in the statistical report. Presenting all results with confidence intervals would have facilitated their interpretation and allowed the effect of the selection of alternative threshold values other than the arbitrarily selected 10 % to be explored. The choice of statistical test should be based on the number of possible outcomes, the use of a series of binomial tests for multinomial distributions would increase the experiment-wise type I error rate (i.e. failure to detect a true adverse effect).

- The statistical analysis should be planned to allow an analysis of the monitoring characteristics according to the length of GM crop cultivation in order to assess residual effects. As the statistical power of the study will be achieved only after 10 years, this will require a pooled analysis. Consequently, when conducting the survey, consideration should be given to the consistency of questions to assess monitoring characteristics, the inclusion of the same farmers in consecutive years in the survey (and the enumeration of these farmers in the report) and the interim analyses performed for the annual reports.

- In situations in which there are three outcomes (of the type: ′*as usual*′ or '*worse*' or '*better*′), it is recommended to use a more appropriate multinomial analysis to test for the distributional difference, with a subsequent binomial approach used to test for differences in a specific category or to correct for the multiplicity of testing. Statistical analysis should also account for the stratified nature of the sample.

- The presentation of the results reported in Appendix 1 of the 2012 PMEM report should be improved in order to facilitate their interpretation.